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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,782	10/01/2003	Simon J. Mantell	PC10921B	8379

28523 7590 07/13/2005

PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/676,782	MANTELL ET AL.
	Examiner	**Art Unit**
	Devesh Khare	1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/29/2005*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

J.O.C

Applicant's request for reconsideration and remarks filed on 04/28/2005 are acknowledged.

The examiner withdraws the rejection of claims 58 and 61 of the office action dated 01/26/2005, under judicially created doctrine of obviousness-type double patenting over U.S. Patent 6,753,322 ('322) in view of U.S. Patent 6,525,032 in response to applicant's remarks that the present application is a divisional of US Patent application serial no. 09/874,007 which issued as the '322 patent.

The examiner revised the rejection of claims 58 and 61 under 35 U.S.C. 112, first paragraph in response to the applicant's comments.

Claims 58 and 61 are currently pending in this application.

Objection

Claims 58 and 61 depend on cancelled claims 1 to 44 and 45.

A correction is required.

35 U.S.C. 112, first paragraph rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 58 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an inflammatory disease with an effective amount of a compound of the formula (I) or with a pharmaceutically acceptable salt, solvate or composition thereof, does not reasonably provide

enablement for septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. It is noted that pages 1-2 of the specification discuss the reasonable correlation between the activity of functional agonists of the human adenosine A2a receptor and that stimulation of A2a receptors to inhibit neutraphil function which act as mediators of inflammation. The specification does not reasonably provide enablement for septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors regarding undue experimentation have been summarized in *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);

(2) The amount of direction or guidance presented;

(3) The presence or absence of working examples of the invention;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The predictability or unpredictability of the art;

(7) The breadth of the claims; and

(8) The relative skill of those in the art.

1. QUANTITY OF EXPERIMENTATION

With regard to factor one the quantity of experimentation needed, undue experimentation is required to determine how to treat diseases such as septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal with an effective amount of adenosine derivative having the Formula I. The absence of specific disclosures or the correlation of data to support applicant's assertions, invites the skilled artisan to engage in undue experimentation, to treat a subject having said disease.

2. GUIDANCE PROVIDED

There is little guidance given in the specification as to the specific treatment of diseases such as septic shock, male erectile dysfunction, male factor infertility, female factor

infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal with an effective amount of adenosine derivative having the Formula I. This lack of guidance would indeed impose the burden of undue experimentation in determining the degree, if any, for the elimination of human health conditions set forth. There is not seen any guidance in the specification drawn to establishing a correlation between the between the activity of functional agonists of the human adenosine A2a receptor and that stimulation of A2a receptors to inhibit neutraphil function which act as mediators of inflammation and the treatment of septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal.

3. <u>WORKING EXAMPLES IN SPECIFICATION</u>

The EXAMPLES advanced in the instant specification are not seen as sufficient to support the breadth of the claims for the treatment of septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal. It is noted that Examples 1-35 and Preparations 1-74 provide the synthesis of said compounds. The pharmacological data provided on page 161 is not sufficient for the treatment of said diseases.

4. <u>NATURE OF THE INVENTION</u>

It is known in this art that certain adenosine derivatives have efficacy in treating specific conditions having an inflammatory disease. The exact mechanism of action and the effects of adenosine derivatives is disclosed (see abstract) (Olsson et al.; J. Of Medicinal Chem. 1986, 29(9), pages 1683-1689; see IDS).

5. <u>STATE OF THE PRIOR ART</u>

The instant claims are drawn to use an effective amount of adenosine derivative having the Formula I in a method for treating a mammal having an inflammatory disease. The following reference is cited to show the state of the prior art:

Olsson et al.; J. Of Medicinal Chem. 1986, 29(9), pages 1683-1689; see IDS.

6. <u>THE PREDICTABILITY OF THE ART</u>

To extrapolate the data presented in the disclosure for the class of compounds of claim 58 and 61 (adenosine derivatives), for the treatment of a mammal having diseases such as septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61, not seen to be enabled or taught in the prior art. Neither the specification nor the prior art provides adequate guidance for equivocating the treatment data for the compounds of claim 58 and 61, for the treatment of a mammal having said diseases.

7. <u>BREATH OF THE CLAIMS</u>

Claims 58 and 61, wherein an effective amount of adenosine derivative having the Formula I, are directed to a method for treating a mammal having an inflammatory

disease. Dependent claim limitations include the diseases such as septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61.

8. THE RELATIVE SKILL IN THE ART

The relative skill in the art as it relates to a method for treating a mammal having an inflammatory disease and the treatment of the diseases such as septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 with an effective amount of adenosine derivative having the Formula I, is that of a Ph.D. or M.D. level.

Presently, the instant specification is not seen to provide an enabling disclosure for the scope of the invention as set forth in claim 61, which encompass for the treatment of septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 with an effective amount of adenosine derivative having the Formula I. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves, see In re Gardner et al. 166 USPQ 138 (CCPA 1970). In the instant case, the amount of experimentation needed to verify a method of treatment of septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy,

cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 with an effective amount of adenosine derivative having the Formula I in a mammal would indeed be voluminous and unduly burdensome in view of the teachings of the instant disclosure.

Rejection Maintained

Applicant's arguments filed on 04/28/05 traversing the rejection of claims 58 and 61 under 35 U.S.C. 112, first paragraph have been fully considered but they are not persuasive.

Response to Arguments

Applicants argue that "page 51-52 discuss an assay demonstrating the anti-inflammatory properties of compounds of formula (I). Pharmacological data corresponding to this assay is reported on page 161".

The absence of specific disclosures or the correlation of data to support applicant's assertions, invites the skilled artisan to engage in undue experimentation. Although applicant alleges that page 51-52 discuss an assay demonstrating the anti-inflammatory properties of compounds of formula (I). Pharmacological data corresponding to this assay is reported on page 161. However, the instant disclosure does not reasonably provide enablement for a method for the treatment of septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury of claim 61 in a mammal with the compounds of formula (I).

The specification, while being enabling for a method of treating an inflammatory disease with an effective amount of a compound of the formula (I) or with a pharmaceutically acceptable salt, solvate or composition thereof, does not reasonably provide enablement for septic shock, male erectile dysfunction, male factor infertility, female factor infertility, hypertension, stroke, epilepsy, cerebral ischaemia, peripheral vascular disease, post-ischaemic reperfusion injury and other diseases listed in claim 61 in a mammal.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is 571-272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Devesh Khare, Ph.D.,JD.
Art Unit 1623
July 11,2005